
Opposing chemokine gradients control human thymocyte migration in situ.

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Public Summary:

The ordered migration of thymocytes from the cortex to the medulla is critical for the appropriate selection of the mature T cell repertoire. Most studies of thymocyte migration rely on mouse models, but we know relatively little about how human thymocytes find their appropriate anatomical niches within the thymus. Here, we examined the intrathymic migration of human thymocytes in both mouse and human thymic stroma and found that human thymocyte subsets localized appropriately to the cortex on mouse thymic stroma and that MHC-dependent interactions between human thymocytes and mouse stroma could maintain the activation and motility of these cells. We also showed that 2 opposing chemokine gradients control the migration of thymocytes from the cortex to the medulla. These findings point to significant interspecies conservation in thymocyte-stroma interactions and provide the first evidence that chemokines not only attract mature thymocytes to the medulla, but also play an active role in retaining thymocytes in the cortex prior to positive selection.

Scientific Abstract:

The ordered migration of thymocytes from the cortex to the medulla is critical for the appropriate selection of the mature T cell repertoire. Most studies of thymocyte migration rely on mouse models, but we know relatively little about how human thymocytes find their appropriate anatomical niches within the thymus. Moreover, the signals that retain CD4⁺CD8⁺ double-positive (DP) thymocytes in the cortex and prevent them from entering the medulla prior to positive selection have not been identified in mice or humans. Here, we examined the intrathymic migration of human thymocytes in both mouse and human thymic stroma and found that human thymocyte subsets localized appropriately to the cortex on mouse thymic stroma and that MHC-dependent interactions between human thymocytes and mouse stroma could maintain the activation and motility of DP cells. We also showed that CXCR4 was required to retain human DP thymocytes in the cortex, whereas CCR7 promoted migration of mature human thymocytes to the medulla. Thus, 2 opposing chemokine gradients control the migration of thymocytes from the cortex to the medulla. These findings point to significant interspecies conservation in thymocyte-stroma interactions and provide the first evidence that chemokines not only attract mature thymocytes to the medulla, but also play an active role in retaining DP thymocytes in the cortex prior to positive selection.

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